UNIVERSITY OF MINNESOTA

Department of Pediatrics
Division of Hematology/Oncology and
Blood & Marrow Transplant Program
John E. Wagner, MD
Division Director

Hematology/Oncology Section
Joseph P. Neglia, MD, MPH
Section Chief

Ashish Kumar, MD, PhD
Daniel Mulrooney, MD, MS
Raj Nagarajan, MD, MS
Marie Steiner, MD, MS
Brenda Weigel, MD

Blood & Marrow Transplant Section
Bruce R. Blazar, MD
Section Chief

K. Scott Baker, MD, MS
Margaret MacMillan, MD
Paul Orchard, MD
Jakub Tolar, MD, PhD
Michael Verneris, MD
John Wagner, MD

Transplant Immunology Program
Bruce R. Blazar, MD
Program Leader

Wei Chen, MD, PhD
Paul Orchard, MD
Angela Panoskaltsis-Mortari, PhD
Jakub Tolar, MD, PhD
Michael Verneris, MD
Xianzheng Zhou, MD, PhD

Metabolic Program
Paul Orchard, MD
Program Leader

Immune Deficiency Program
K. Scott Baker, MD, MS
Program Leader

Fanconi Anemia Comprehensive Clinic
Margaret MacMillan, MD / John Wagner, MD
Co-Program Leaders

Experimental Therapeutics Program
Brenda Weigel, MD / John Wagner, MD
Co-Program Leaders

Thrombosis/Hemostasis Program
Marie Steiner, MD, MS
Program Leader

CCRF Long-Term Follow-Up Clinic
Daniel Mulrooney, MD, MS
Program Leader

Hematology/Oncology
Clinic (612) 625-5411
Referrals (612) 626-2778

Blood & Marrow Transplant
Clinic (612) 626-2663
Referrals (612) 626-2961

CCRF Long-Term Follow-Up Clinic
Referrals
(612) 626-2778

Fanconi Anemia Comprehensive Clinic
Referrals (612) 626-2961

Division Office
Cancer Center Research Building
425 East River Road - Suite 660
Minneapolis, MN 55455
Phone (612) 626-2961
Fax (612) 626-4074
www.med.umn.edu/peds/bmt/
www.med.umn.edu/peds/hemonc/

NCI® A Comprehensive Cancer Center Designed by the National Cancer Institute
CCC

Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, of the Committee on Appropriations

"The Potential of Stem Cell and Nuclear Transplantation Research."

Wednesday, October 19, 2005, Dirksen Senate Office Building
John E. Wagner, M.D., University of Minnesota
Scientific Director of Clinical Research
Blood and Marrow Transplant Program and Stem Cell Institute

Stem Cells: A Clinician's Perspective on Embryonic Stem Cell Research

Stem cell therapy will revolutionize the practice of medicine. For the first time there will be treatments for spinal cord injury, diabetes, cancer, stroke, and heart disease with potentially long term benefits. The proof of principle already exists.

It is not a question of whether this new knowledge will 'translate' into clinical therapies but rather how long. Will clinical trials in diabetes or stroke be soon or decades away? Will this work be driven by private industry without any oversight or in academic environments using federal support; conducted in university settings which guarantee requisite oversight, publication, peer review and transparency?

So what do we know about stem cells today?

There is only one proven established use of stem cells and that is in the setting of bone marrow transplantation. For decades it has been known that marrow stem cells can be transplanted from one individual to another in order to replace the blood and marrow of patients with leukemia/lymphoma/multiple myeloma/other diseases after their own marrow has been destroyed by disease or treatment with high doses of chemotherapy and radiation. These stem cells come from adult marrow or umbilical cord blood.

My own work is focused on umbilical cord blood and development of novel phase I clinical trials. In this discussion, we cannot forget that cord blood is already an established treatment with tremendous potential. Recently, the Institute of Medicine summarized its findings on the benefits of cord blood and the urgent need to expand the useable inventory. Cord blood is rapidly becoming the standard of care in children. We have recently reported outcomes in adults with results

that are unprecedented. However, it must be clear that cord blood stem cells are not the stem cells found in embryonic stem cell lines. The stem cells in adult tissues and umbilical cord blood have different properties and may or may not have unlimited differentiation capacity. While it is hoped that one day we will be able to take adult tissue or cord blood stem cells and trick it to become 'ES-like', this is not yet possible. Despite what the opponents to ES cell work would suggest, it is simply not true.

The University of Minnesota is well known in the field of stem cell research. We have the longest standing Stem Cell Institute in the country. My work in umbilical cord blood stem cell research and Catherine Verfaillie's work on the multipotent adult stem cell clearly demonstrate our hope to maximize the potential of cord blood and adult tissue stem cells but we recognize that there are limitations. Of course we are excited about the future potential of these stem cells but never have we suggested that they obviate the need for ES cell research. For example, never have the stem cells from cord blood or adult tissues ever produced heart muscle cells that spontaneously beat or formed islets that secrete insulin, as has been shown repeatedly with ES.

It is critical for the public to know that if we are ever to make cord blood and adult tissue stem cells function like ES cells, we need to study ES cells. Every discovery with ES cells has furthered our work with stem cells from umbilical cord blood or adult tissues.

Now speaking as a clinician who actually performs new therapies with stems cells in humans, we are indeed planning to perform the first clinical trial with multipotent adult stem cells this winter in an attempt to repair tissues damaged by radiation and chemotherapy. My goal is to move stem cell therapy forward in numerous areas as the clinical director of the Stem Cell Institute. Once we meet the requirements of the Human Subjects Committee, FDA, Ethics committees, we plan to move stem cell therapies forward regardless of whether they are ES, cord blood or adult tissue-derived. It is incomprehensible to do otherwise. Like others, I receive thousands of letters, emails, phone calls per month asking me to allow them to be the first to receive stem cell treatments — these people have cancer, spinal cord injury, diabetes, strokes, Parkinson's disease, and other genetic diseases. (Show sample emails from this week).

You ask, what is the future of ES cells to cure a disease – the answer is simply "breathtaking". Clearly there are risks as ES cells if left undifferentiated have a propensity to cause tumors. But still, many are working to make these cells therapeutically valuable. In addition to the development of novel strategies for treating Parkinson's, diabetes, stroke and spinal cord injury, some like Daniel Kaufman at the University of Minnesota are focused on manufacturing red blood cells in massive scale thus reducing our dependence upon volunteer donors or developing nature killer cells as anti-cancer agents-both derived from ES cells. So why has there not been a single trial thus far with ES cell – funding, access to suitable cells lines, and research on the immune response to these stem cells. Nuclear transfer will be crucial to this success – "tailor made" stem cells lines for individuals will be required to counter likely immune responses. Again, this is not futuristic, the South Korean scientists have clearly demonstrated that this is not just desirable but possible.

To restrict work with ES cells or bar SCNT would cripple our capacity to move all stem cell therapies forward ES cells are the gold standard and research with them will maximize the potential of cord blood and adult stem cells and pursuit of multiple approaches will permit the most rapid translation of stem cells possible into efficacious clinical therapies. Every single one of us will be faced with a child, friend, loved one, or even ourselves with a disease amenable to stem cell therapy in the not too distance future. Umbilical cord blood has proven benefits in the treatment of leukemia, lymphoma, blood disorders, immune deficiencies and metabolic diseases today. Banking of cord blood is in the nation's interest and federal dollars should continue to be spent to determine the breadth of what it can offer well beyond the confines of blood and marrow diseases. At the same time in parallel, we must also push ES and adult stem cells to the limits of what they can offer. And for ES cells, banning SCNT could prevent its future success as SCNT is likely to be the key that will make ES cell therapies more widely available more rapidly. I am here as an advocate for the thousands of people who have asked me to push this forward.